FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Joint Meeting of the Pulmonary-Allergy Drugs Advisory Committee (PADAC) & Drug Safety and Risk Management (DSaRM) Advisory Committee
March 10-11, 2010

Hilton Washington, DC North/ Silver Spring
8727 Colesville Road, Silver Spring, MD

Draft Questions to the Committees

Study Endpoints

1. A composite safety endpoint of asthma-related hospitalizations, asthma-related intubations, and asthma-related deaths is proposed for the adult/adolescent safety study.

Discuss:

a) The adequacy of the primary endpoint to address the safety concerns of LABAs for the treatment of asthma in adults/adolescents

b) What level of risk for LABAs would be considered acceptable to rule out; i.e., what would be an acceptable upper bound of the 95% confidence interval?

c) Alternative endpoints that could be considered to evaluate the safety of LABAs for the treatment of asthma in adults/adolescents

2. A safety endpoint of asthma-related hospitalizations is proposed for the pediatric safety study.

Discuss:

a) The adequacy of the primary endpoint to address the safety concerns of LABAs for the treatment of asthma in pediatrics

b) What level of risk for LABAs would be considered acceptable to rule out; i.e., what would be an acceptable upper bound of the 95% confidence interval?

c) Alternative endpoints that could be considered to evaluate the safety of LABAs for the treatment of asthma in pediatrics

Study Design

3. Given the hypothesis to be tested, discuss the advantages and disadvantages of a study design with a "real world" approach where patients enrolled are allowed titration of the

inhaled corticosteroid (ICS) dose compared to a study design where the dose of ICS remains fixed. Which of these designs would be more appropriate to address the safety concerns of LABAs for the treatment of asthma?

a) in adults/adolescents
b) in pediatrics

4. For a study design where the ICS dose remains fixed, discuss whether the ICS dose should be the same in the treatment arms or whether the ICS monotherapy group should have a higher dose.

Length of Exposure

5. Discuss the adequacy of a 6 to 12 month treatment period to address the safety concerns of LABAs for the treatment of asthma

a) in adults/adolescents
b) in pediatrics
c) Discuss the advantages and disadvantages of a shorter treatment period e.g. 3 months

Additional Questions

1. Discuss what would be a reasonable timeframe for completion of the safety study.

2. Given that data from the SMART study suggest a higher safety signal in African-Americans, and national statistics indicate a higher rate of serious asthma outcomes in the African-American population, a representative number of African-Americans are proposed for inclusion in the U.S. study sites. Discuss the challenges for obtaining meaningful information from sub-group analyses from the proposed study and possible options to address them.